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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/526,582	03/16/00	FITZPATRICK J	SRX 110

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EXAMINER	
GABEL,G	
ART UNIT	PAPER NUMBER
1641	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/526,582	FITZPATRICK ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

Abstract

1. Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art. Specifically, the last 2 lines of the Abstract of the Disclosure makes reference to prior art which should appropriately be incorporated into the Background of the Invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. It is unclear how detection of immunoreactivity is effected in the absence of a label and/or other reagents.

Claim 1 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: detection and correlation step.

Claim 1 is vague and indefinite in reciting "detection of lipoprotein comprising saliva with antibodies" because the claim implies but does not specifically recite that the apolipoproteins in question are being detected are from the saliva.

In claim 4, change "lable" to "label".

Claim 6 is vague and indefinite in reciting "wherein the saliva is prepared ... to remove mucopolysaccharides" because it implies but does not specifically recite that the method encompasses "removing the mucopolysaccharides from the saliva".

Claim 7 is ambiguous in reciting "saliva is collected after stimulation" because it fails to specifically define what is being encompassed by the term "stimulation" as recited in the claim.

Claim 8 is incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. It is unclear how determination

of albumin is effected in the absence of antibodies, a label, and/or other reagents in the instant claim and claim 1 from which it depends.

Claim 9 is ambiguous in reciting "normalizing the amount of apolipoprotein to the amount of albumin present" because it is unclear what Applicant intends to encompass in reciting "normalizing" as used in the claim.

Claim 9 has improper antecedent basis problems in reciting "apolipoprotein" and "albumin". Change to "the apolipoprotein" and "the albumin" for proper antecedent basis.

Claim 10 has improper antecedent basis problems in reciting "mucopolysaccharides", "antibodies", and "of apolipoprotein". Change to "the mucopolysaccharides", "the antibodies", and "of the apolipoprotein" for proper antecedent basis.

Claim 12 is incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. It is unclear how detection of immunoreactivity is effected in the absence of a label.

Claim 16 is indefinite in reciting "The device or kit wherein" because it fails to recite the claim from which it depends. Alternatively, if meant to be an independent claim, claim 16 has improper antecedent basis problem.

Claim 16 lacks clear antecedent support in reciting "the antibodies". For example, does Applicant intend "antibodies immunoreactive to apolipoprotein" or "to albumin".

Claim 16 is ambiguous in reciting "the antibodies are contained on" because it is unclear what Applicant intends to encompass in reciting "contained on" as used in the claim as compared to "immobilized on".

Claim 17 is indefinite in reciting "The device or kit comprising" because it fails to recite the claim from which it depends. Alternatively, if meant to be an independent claim, claim 17 has improper antecedent basis problem.

Claim 18 is indefinite in reciting "The device or kit comprising" because it fails to recite the claim from which it depends. Alternatively, if meant to be an independent claim, claim 18 has improper antecedent basis problem.

Claim 19 is confusing in reciting "comprising as separate reagents antibodies to an apolipoprotein and antibodies to albumin". Perhaps, changing to "comprising a reagent consisting of antibodies to an apolipoprotein and a reagent consisting of antibodies to albumin" will assist in clarifying the claim.

Claim 19 is indefinite in reciting "The device or kit comprising" because it fails to recite the claim from which it depends. Alternatively, if meant to be an independent claim, claim 19 has improper antecedent basis problem.

Claim 20 is incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. It is unclear how detection of immunoreactivity is effected in the absence of a label and/or other reagents.

Claim 20 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: detection and

correlation step leading to the diagnostic presence of lipid disorders and risk of cardiovascular disease.

Claim 20 is confusing because it is not clear what the method is attempting to quantitate, i.e. 1) amount of lipoprotein or cholesterol in saliva; 2) presence of lipid disorders; or 3) risk of cardiovascular disease? If Applicant intends to quantitate 2) and 3), it is unclear how quantitation of the presence or risk of a disease is effected.

Claim Rejections - 35 USC § 102

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-3, 12, 14, 16-18, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by 1) Oberhardt (US 5,677,133).

Oberhardt discloses an immunoassay for detection of apolipoproteins such as apo-A1 and apo B-100 on difficult biological samples such as saliva (see column 3, lines 24-31 and column 4, lines 11-16). Specifically, Oberhardt discloses reacting the sample with a dry reagent containing antibodies immunoreactive to the apolipoproteins, the apolipoproteins (analyte) bound to a reaction cascade initiator, and magnetic particles to form a reaction mixture (see column 5, lines 47-64). Thereafter, Oberhardt discloses applying oscillating or moving static magnetic field to the reaction mixture to activate the reaction cascade initiator, monitoring the response of the magnetic particles to provide a signal, then determining the concentration of the apolipoprotein based on

the signal (see also column 14, line 50 bridging to column 15, line 44). Depending on the assay, other reagent components may be included and used with the dry reagent such as buffers and neutralizers (see column 6, lines 39-44). The immunoassay is performed on a strip or dipstick (reaction slide) (see column 6, lines 4-29). Oberhardt discloses application of the invention to a panel of affinity assays or immunoassay for different but related analytes in single application of the sample to the reaction slide by utilizing different reaction elements and reagent components (see column 4, lines 34-43).

4. Claims 1-3, 12, 14, 16-18, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by 2) Oberhardt (US 5,601,991).

Oberhardt discloses an immunoassay for detection of apolipopropteins such as apo-A1 and apo B-100 on difficult biological samples such as saliva (see column 3, lines 26-33 and column 4, lines 14-19). Specifically, Oberhardt discloses reacting the sample with a dry reagent containing antibodies immunoreactive to the apolipoproteins, the apolipoproteins (analyte) bound to a reaction cascade initiator, and magnetic particles to form a reaction mixture (see column 4, lines 52-67 and claims 39-40). Thereafter, Oberhardt discloses applying oscillating or moving static magnetic field to the reaction mixture to activate the reaction cascade initiator, monitoring the response of the magnetic particles to provide a signal, then determining the concentration of the apolipoprotein based on the signal (see also column 14, line 53 bridging to column 15, line 42). The immunoassay is performed on a strip or dipstick (reaction slide) (see

column 6, lines 8-33). Depending on the assay, the dry reagent and all reagent components including buffers and neutralizers may be incorporated into a kit format (see claims 34-37).

5. Claims 1 and 4 are rejected under 35 U.S.C. 102(e) as being anticipated by Kundu et al. (US 6,210,906).

Kundu et al. disclose detecting apolipoprotein A in a saliva sample using labeled monoclonal antibodies against kringle 5 domain of apolipoprotein A (see Abstract, column 4, lines 39-52, and column 8, lines 8-15). Kundu et al. disclose labeling the antibodies using chromogen, fluorescent compounds, radioactive labels, etc. (see column 9, lines 57-67).

6. Claims 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Ullman et al. (US 5,137,808).

Ullman et al. disclose a device or kit with a solid support comprising bibulous material onto which receptors and antibodies are immobilized (see Abstract).

7. Claims 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Kang (US 5,559,041).

Kang et al. disclose a device or kit with a solid support onto which antibodies are immobilized (see column 2, lines 46-52 and Figures 4 and 6).

8. Claims 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (US 5,384,264).

Chen et al. disclose a device or kit with a solid support onto which antibodies (antiligands) are immobilized (see Abstract).

9. Claims 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by May et al. (US 5,602,040).

May et al. disclose a test strip in a kit with a solid support onto which antibodies (antiligands) are immobilized (see Abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 5-7, 10, 11, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oberhardt (US 5,677,133) or Oberhardt (US 5,601,991) in view of Fellman et al. (US 5,112,758).

1) Oberhardt and 2) Oberhardt have been discussed supra. 1) Oberhardt and 2) Oberhardt differ in failing to specifically disclose removing mucopolysaccharides from saliva prior to diagnostic testing.

Fellman et al. disclose a method and kit for stimulating saliva production (inducing salivation) in a subject using a sour stick (ascorbic acid) (see column 3, lines 45-61). Fellman et al. also teach a method of treating saliva prior to diagnostic testing using cationic quaternary ammonium reagents. Specifically, Fellman et al. disclose that centrifugation and filtration are known techniques for removing mucopolysaccharides from saliva. According to Fellman et al., viscosity reduction is necessary for the preparation of body fluids containing mucopolysaccharides for accuracy in testing, i.e. detecting for presence of antibodies and antigen (see column 1 and 4).

One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the teaching of Fellman in removing mucopolysaccharides to reduce viscosity of a specimen into the methods taught by 1) Oberhardt and 2) Oberhardt in detecting apolipoproteins in the saliva because Fellman specifically taught that removal of this excess element decreases background noise

which prevents useful detection of analyte such as the apolipoproteins in the method of 1) Oberhardt and 2) Oberhardt (see Fellman et al., column 3, lines 15-25).

1) Oberhardt , 2) Oberhardt, and Fellman fail to disclose that saliva is tested in less than 3 hours after collection such as recited in claim 5.

However, it is maintained that parameters, such as time requirements for collection and analysis of biological specimen that affect viability of biological components or efficacy of reagents, are all result effective variables which the prior art references have shown may be altered in order to achieve optimum results. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitation recited in instant claim 5 is for any particular purpose or solve any stated problem, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of time collection and analysis requirements of the methods disclosed by 1) Oberhardt , 2) Oberhardt, and Fellman by normal optimization procedures.

11. Claims 7-9, 15, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oberhardt (US 5,677,133) or Oberhardt (US 5,601,991) in view of

Fisher et al. (Diabetes Research and Clinical Practice, 1991 (Abstract)) and Coppo et al. (Journal of Diabetic Complications, 1987 (Abstract)).

1) Oberhardt and 2) Oberhardt have been discussed supra. 1) Oberhardt and 2) Oberhardt differ in failing to teach determining the amount of albumin in the saliva and normalizing the amount of apolipoprotein to the amount of albumin present in the saliva. 1) Oberhardt and 2) Oberhardt further differ in failing to teach incorporating antibodies immunoreactive to albumin in the device or kit for determining apolipoprotein concentration.

Fisher et al. teach that the concentration of albumin in saliva is low in healthy humans. Fisher et al. teach using citric acid to stimulate saliva secretion then measuring its albumin level using ELISA method. Fisher et al. compare albumin concentration between saliva and urine in diabetes patients.

Coppo et al. teach determining urinary albumin concentrations using anti-albumin antibody in an indirect ELISA technique.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Coppo in using anti-albumin antibodies to measure the level of albumin in a body fluid such as urine using ELISA technique or saliva such as in the ELISA method taught by Fisher, into the method and device taught by 1) Oberhardt or 2) Oberhardt because 1) Oberhardt and 2) Oberhardt specifically suggested application of their kit and method in multianalyte or panel screening applications for any antigen combination present in body fluids, such as apolipoproteins and albumin present in saliva, using respective immunoreactive antibodies that are

specific thereto. Further, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the reagents, labels and immunoreactive antibodies specific for albumin in the method taught by Coppo into a kit arrangement because test kits are conventional and well known in the art for their recognized advantages of convenience and economy.

It further would have been prima facie obvious to one of ordinary skill in the art to perform statistical evaluation of concentration levels between coexisting analytes present in a body fluid and effect correction, if necessary, to remove effects of possible interference or dilution, so that an actual concentration of the desired analyte is obtained since statistical correction methods are standard in laboratory practice during optimization procedures.

12. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Coppo et al. (Journal of Diabetic Complications, 1987 (Abstract)) in view of Kang (US 5,559,041) or Chen et al. (US 5,384,264) or May et al. (US 5,602,040) or Ullman et al. (US 5,137,808).

Coppo et al. has been discussed supra. Coppo et al. fail to incorporate the anti-albumin antibodies and ELISA reagents into a kit format.

Kang et al. , Chen et al., May et al., and Ullman et al. have been discussed supra.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the ELISA reagents and immunoreactive antibodies

specific for albumin in the method taught by Coppo into a kit arrangement such as disclosed by Kang, Chen, May, and Ullman because test kits are conventional and well known in the art for their recognized advantages of convenience and economy.

13. No claims are allowed.

Remarks

14. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Aronowitz (WO 94/12879) disclose a dry reagent three element analyte detection system.

Fitzpatrick et al. (US 5,451,504) disclose a membrane strip for detecting analyte from biological samples such as saliva. The membrane strip has a mobilization zone, a trap zone, and a detection zone.

Messenger et al. (US 5,162,237) disclose a reaction cassette for performing sequential analytical assays by noncentrifugal and noncapillary manipulations.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
June 29, 2001

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800 /641